



Bristol-Myers Squibb Company

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August 5, 2004

**Dockets Management Branch
Food and Drug Administration, HFA-305
5630 Fishers Lane, Room 1061
Rockville, MD 20852**

Re: Docket No. 97D-0299 Proposed ICH Guidance Question and Answer: *E5 - Ethnic Factors in the Acceptability of Foreign Clinical Data – Questions and Answers*

Dear Sir or Madam:

Bristol-Myers Squibb Company (BMS), a diversified worldwide health and personal care company with principal businesses in pharmaceuticals, infant formulas, and nutritional products, is pleased to have the opportunity to offer comments on the ICH E5 - Ethnic Factors in the Acceptability of Foreign Clinical Data – Questions and Answers document. BMS' mission is to extend and enhance human life by providing the highest-quality pharmaceutical and related health care products. For this reason, we are interested in commenting on the above ICH E5 Guidance - Question and Answers document. Our comments are set forth below.

General Comments

We commend the FDA for providing a useful document that in conjunction with the guidance itself, will efficiently assist applicants in evaluating the impact of ethnic factors in the acceptability of foreign clinical data. We have no comments on what FDA has drafted. However, we would like to propose several additional questions which may help provide better direction to applicants on the practical implementation of ICH E5 Guidance in global drug development.

Specific Comments

Listed below are additional questions we suggest be incorporated into this Question and Answer document in order to provide further clarifications to the applicants:

- 1) Does the lack of difference in intrinsic ethnic factors need to be prospectively demonstrated, even in the case when a drug can be categorized as "ethnically insensitive"?
- 2) What characteristics need to be met for a population in the foreign region to be representative of the new region? In Appendix C, there is mention of three major racial groups; can further definition be provided on these?

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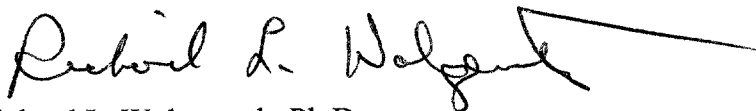
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- 3) In the case a bridging study needs to be conducted in the new region, is it always necessary to demonstrate PK similarity in both populations before proceeding to collect PD or clinical data to demonstrate similar efficacy, safety, dosage and dose regimen, in order to be able to extrapolate data to a new region?
- 4) Under what circumstances is a dose response study not required to be conducted in the new region in order to establish that the same dose and dose regimen apply in the new region?
Can the bridging be demonstrated via the conduct of a) a single dose study or b) the participation of the new region in a global (phase III) study with a single dose, including the foreign and new region, without the need to conduct dose response studies in both regions?
- 5) Can examples be given to illustrate situations when there are doubts about the choice of dose (in reference to section 3.2.3 of the guidance)?
- 6) Regarding the design for the bridging study, is it necessary for the bridging study to have the same design as a study conducted in the foreign region in order to be able to establish the similarity in effect and thus the ability to extrapolate?
- 7) Can more guidance be provided on the definition of "similar" efficacy, safety, dosage, and dose regimen which fulfill the ability to bridge? Are there statistical aspects that need to be considered in order to establish this similarity across studies in both regions?

BMS appreciates the opportunity to provide comment and respectfully requests that FDA give consideration to our recommendations. We would be pleased to provide additional pertinent information as may be requested.

Sincerely,



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